L Number	Hits	Search Text	DB	Time stamp
1	2724	("514/183,212.05,214.02,214.03,286,288").CCLS	USPAT	2004/08/25 08:25
2	1964	("540/468,472,477,544,556,576,596,604").CCLS	USPAT	2004/08/25 08:26
3	171	("546/63").CCLS	USPAT	2004/08/25 08:26
4	298	("548/421,424,425").CCLS	USPAT	2004/08/25 08:27
5	18	L1and (("540/468,472,477,544,556,576,596,604").CCLS) and (("546/63").CCLS) and (("548/421,424,425").CCLS)	USPAT	2004/08/25 08:27

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LOGINID:ssspta1611sxp

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	May 12	EXTEND option available in structure searching
NEWS	4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS	5	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS	6	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS	7	Jun 28	Additional enzyme-catalyzed reactions added to CASREACT
NEWS	8	Jun 28	ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG, and WATER from CSA now available on STN(R)
NEWS	9	Jul 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS	10	Jul 30	BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting
NEWS	11	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS	12	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS	13	AUG 02	STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting
NEWS	14	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS	15	AUG 04	Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:37:36 ON 25 AUG 2004

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=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:37:46 ON 25 AUG 2004
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STRUCTURE FILE UPDATES:   24 AUG 2004  HIGHEST RN 732209-96-0
DICTIONARY FILE UPDATES:  24 AUG 2004  HIGHEST RN 732209-96-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10784064.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
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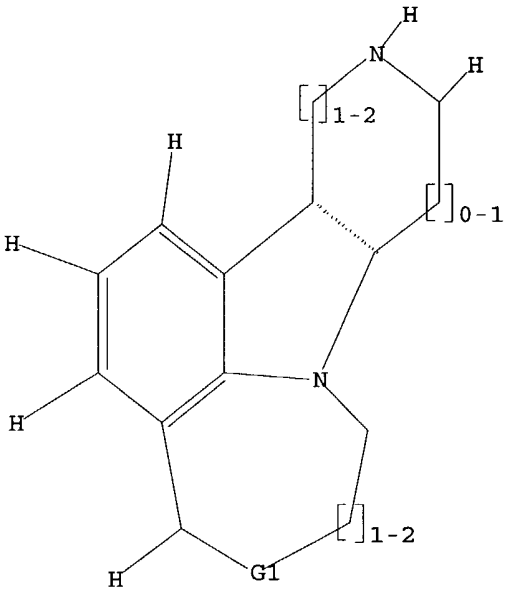

G1 O,S,N,SO2,NH

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full
FULL SEARCH INITIATED 08:38:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 94309 TO ITERATE

100.0% PROCESSED 94309 ITERATIONS 15 ANSWERS
SEARCH TIME: 00.00.01

L2 15 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.42	155.63

FILE 'CAPLUS' ENTERED AT 08:38:23 ON 25 AUG 2004
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FILE COVERS 1907 - 25 Aug 2004 VOL 141 ISS 9
FILE LAST UPDATED: 24 Aug 2004 (20040824/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2
L3 3 L2

=> d l3 fbib hitstr abs total

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:575087 CAPLUS
DN 137:140432
TI Preparation of pyridoindoles as human serotonin receptor 5-HT2C agonists and 5-HT2A antagonists
IN Robichaud, Albert J.; Fevig, John M.; Mitchell, Ian S.; Lee, Taekyu; Chen, Wenting; Cacciola, Joseph
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 409 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI	WO 2002059129	A2	20020801	WO 2001-US49371		20011219
	WO 2002059129	A3	20030130			
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
				US 2000-256740P	P	20001220
	US 2002173503	A1	20021121	US 2001-26611		20011219
	US 6699852	B2	20040302			
				US 2000-256740P	P	20001220
	EP 1343791	A2	20030917	EP 2001-994316		20011219
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				US 2000-256740P	P	20001220
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	NO 2003002797	A	20030819	NO 2003-2797		20030619
				US 2000-256740P	P	20001220
				WO 2001-US49371	W	20011219

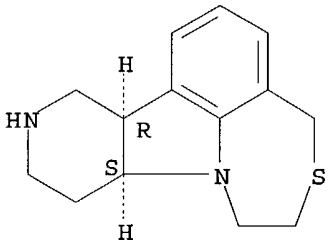
OS MARPAT 137:140432
IT **444718-70-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of pyridoindoles as human serotonin receptor

5-HT2C agonists and 5-HT2A antagonists)
RN 444718-70-1 CAPLUS
CN 4H-Pyrido[3',4':4,5]pyrrolo[3,2,1-jk][4,1]benzothiazepine, 1,2,7b,8,9,10,11,11a-octahydro-, (7bR,11aS)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 444718-69-8
CMF C14 H18 N2 S

Absolute stereochemistry.



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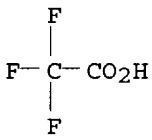
CRN 76-05-1
CMF C2 H F3 O2

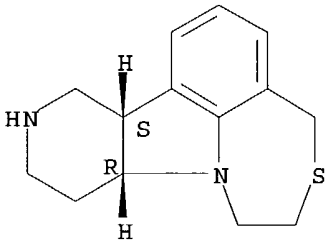


IT **444718-73-4P 444718-76-7P 444719-37-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyridoindoles as human serotonin receptor 5-HT2C agonists and 5-HT2A antagonists)
RN 444718-73-4 CAPLUS
CN 4H-Pyrido[3',4':4,5]pyrrolo[3,2,1-jk][4,1]benzothiazepine, 1,2,7b,8,9,10,11,11a-octahydro-, (7bS,11aR)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

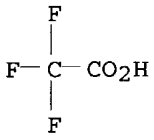
CRN 444718-72-3
CMF C14 H18 N2 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

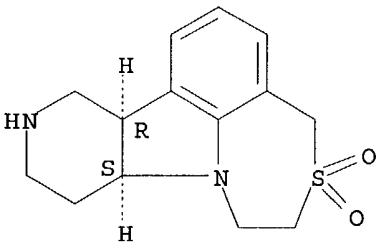


RN 444718-76-7 CAPLUS
CN 4H-Pyrido[3',4':4,5]pyrrolo[3,2,1-jk][4,1]benzothiazepine, 1,2,7b,8,9,10,11,11a-octahydro-, 3,3-dioxide, (7bR,11aS)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 444718-75-6
CMF C14 H18 N2 O2 S

Absolute stereochemistry.



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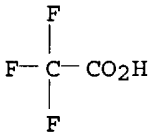
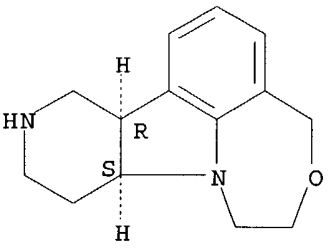


RN 444719-37-3 CAPLUS
CN 4H-Pyrido[3',4':4,5]pyrrolo[3,2,1-jk][4,1]benzoxazepine, 1,2,7b,8,9,10,11,11a-octahydro-, (7bR,11aS)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 444719-36-2
CMF C14 H18 N2 O

Absolute stereochemistry.



CM 2

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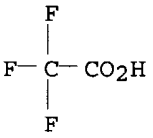
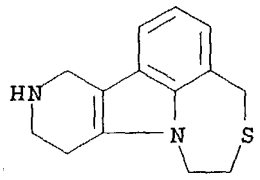
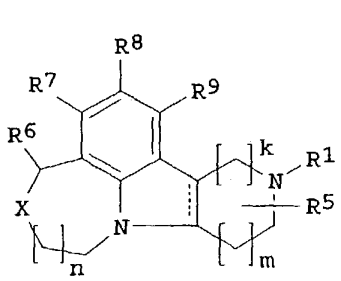


IT **444721-61-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyridoindoles as human serotonin receptor 5-HT2C agonists and 5-HT2A antagonists)
RN 444721-61-3 CAPLUS
CN 4H-Pyrido[3',4':4,5]pyrrolo[3,2,1-jk][4,1]benzothiazepine, 1,2,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)



GI



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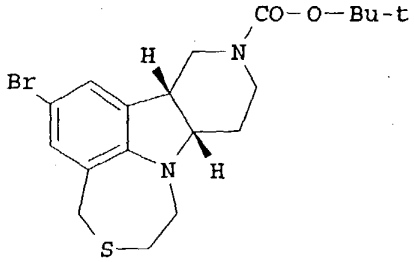
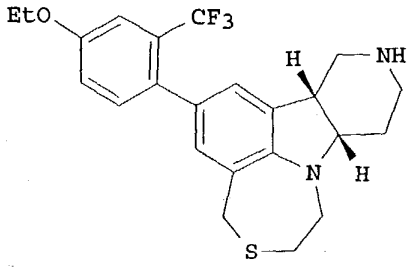


II



II

AB Title compds. I and their pharmaceutically acceptable salts [R1 = H, alkyl, alkenyl, alkynyl, etc.; R5, R6 = H, alkyl; R7, R8, R9 = H, halo, CF3, aryl etc.; k, n = 1, 2; m = 0, 1; X = O, S, SO, etc.] and formulations were prepared For example, Suzuki coupling of chiral bromide II, e.g., prepared in 7 steps from 1,5-dihydro-4,1-benzothiazepin-2(3H)-one, and 4-ethoxy-2-trifluoromethylphenyl boronic acid, followed by BOC deprotection afforded pyridothiazepinoindole.TFA III. In vitro radioligand binding assays, compds. I had IC50 values < 50 μM for 5-HT2A antagonism or 5-HT2C agonism. Compds. I are useful in the control or prevention of central nervous system, sexual, gastrointestinal disorders etc..

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NEWS 12	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 13	AUG 02	STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting
NEWS 14	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 15	AUG 04	Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:42:21 ON 25 AUG 2004

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:42:33 ON 25 AUG 2004
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STRUCTURE FILE UPDATES:   24 AUG 2004  HIGHEST RN 732209-96-0
DICTIONARY FILE UPDATES:  24 AUG 2004  HIGHEST RN 732209-96-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading c:\program files\stnexp\queries\10784064.1

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
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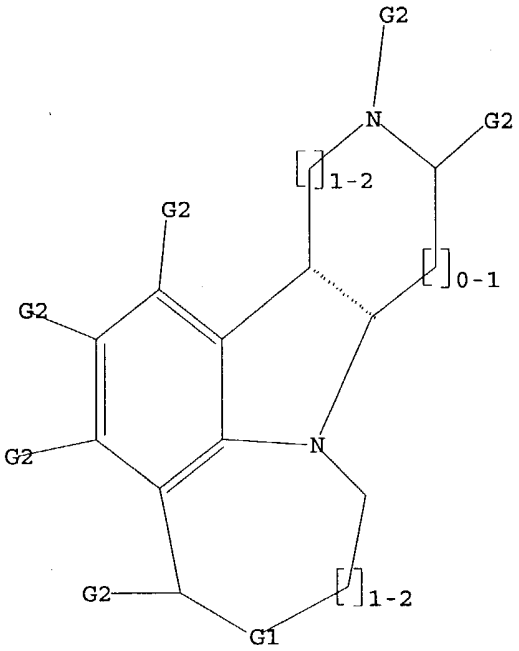

G1 O,S,N,SO2,NH

G2 H,Ak

Structure attributes must be viewed using STN Express query preparation.

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FULL SEARCH INITIATED 08:42:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 94309 TO ITERATE

100.0% PROCESSED 94309 ITERATIONS 37 ANSWERS
SEARCH TIME: 00.00.02

L2 37 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.42	155.63

FILE 'CAPLUS' ENTERED AT 08:43:04 ON 25 AUG 2004
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FILE COVERS 1907 - 25 Aug 2004 VOL 141 ISS 9
FILE LAST UPDATED: 24 Aug 2004 (20040824/ED)

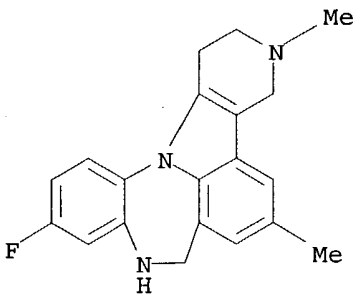
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L3 NOT FOUND
The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l2
L3 7 L2

=> d l3 fbib hitstr abs total

L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:806855 CAPLUS
DN 138:362042
TI Predicting drug-induced agranulocytosis: characterizing neutrophil-generated metabolites of a model compound, DMP 406, and assessing the relevance of an in vitro apoptosis assay for identifying drugs that may cause agranulocytosis
AU Iverson, S.; Zahid, N.; Uetrecht, J. P.
CS Faculty of Pharmacy, University of Toronto, Toronto, M5S 2S2, Can.
SO Chemico-Biological Interactions (2002), 142(1-2), 175-199
CODEN: CBINA8; ISSN: 0009-2797
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
IT **227030-51-5D**, DMP 406, reactive metabolites
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(characterizing neutrophil-generated metabolites of DMP 406 and assessing the relevance of an in vitro apoptosis assay for identifying drugs that may cause agranulocytosis)
RN 227030-51-5 CAPLUS
CN Benzo[b]pyrido[3',4':4,5]pyrrolo[3,2,1-jk][1,4]benzodiazepine, 11-fluoro-1,2,3,4,8,9-hexahydro-3,6-dimethyl- (9CI) (CA INDEX NAME)

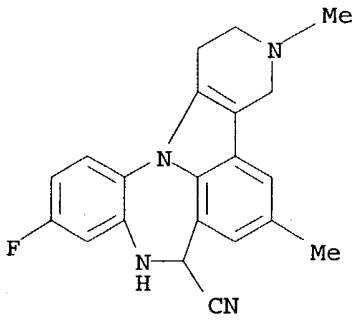


IT **524678-82-8P**

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(characterizing neutrophil-generated metabolites of DMP 406 and assessing the relevance of an in vitro apoptosis assay for identifying drugs that may cause agranulocytosis)

RN 524678-82-8 CAPLUS

CN Benzo[b]pyrido[3',4':4,5]pyrrolo[3,2,1-jk][1,4]benzodiazepine-8-carbonitrile, 11-fluoro-1,2,3,4,8,9-hexahydro-3,6-dimethyl- (9CI) (CA INDEX NAME)

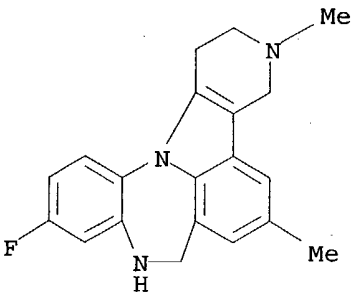


IT **227030-51-5**, DMP 406

RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(characterizing neutrophil-generated metabolites of DMP 406 and mianserin and assessing the relevance of an in vitro neutrophil-generated apoptosis assay for identifying drugs that may cause agranulocytosis)

RN 227030-51-5 CAPLUS

CN Benzo[b]pyrido[3',4':4,5]pyrrolo[3,2,1-jk][1,4]benzodiazepine, 11-fluoro-1,2,3,4,8,9-hexahydro-3,6-dimethyl- (9CI) (CA INDEX NAME)



AB DMP 406 is a clozapine analog developed by Dupont-Pharma for the treatment of schizophrenia. Unfortunately it caused agranulocytosis in dogs during preclin. studies. Clozapine also causes agranulocytosis and this is believed to be due to a reactive nitrenium ion metabolite produced by neutrophils. We studied the oxidation of DMP 406 by activated neutrophils and found that the major reactive species that is produced is not a nitrenium ion but rather an imine. This metabolite is similar to the reactive metabolite that has been proposed to be responsible for mianserin-induced agranulocytosis. Therefore we also studied the oxidation

of mianserin by activated neutrophils and found that, although the major species is an iminium ion, it also bears a lactam moiety in the piperazine ring resulting from further oxidation We usually find that HOCl is a good model system for the production of reactive metabolites of drugs that are formed by activated neutrophils, but in the case of both DMP 406 and mianserin, the products produced were significantly different than those formed by activated neutrophils. In contrast, the combination of horseradish peroxidase and hydrogen peroxide (HRP/H2O2) formed a very similar pattern of products, and this system was used to produce sufficient quantities of metabolites to allow for identification. The reactive metabolites of both DMP 406 and mianserin reacted with a range of nucleophiles, but in many cases the reaction was reversible. The best nucleophile for trapping these reactive metabolites was cyanide. It has been demonstrated that the products of clozapine oxidation by HRP/H2O2, presumably the nitrenium ion, induced apoptosis in neutrophils at therapeutic concns. of clozapine. It has been suggested that this process is involved in the mechanism of clozapine-induced agranulocytosis. We tested DMP 406 and mianserin in this system to see if the ability of a reactive metabolite of a drug to cause apoptosis could predict the ability of that drug to cause agranulocytosis. We used clozapine as a pos. control and we also tested olanzapine, a drug that forms a reactive metabolite similar to that of clozapine but is given at a lower dose and does not cause agranulocytosis. We found that DMP 406 did not increase apoptosis at concns. below 50 μM, and although mianserin did increase apoptosis at 10 μM this is above the therapeutic concentration Olanzapine caused an increase in apoptosis at the same concentration as clozapine (1 μM), but because its therapeutic concentration is lower, this concentration was above the pharmacol. range. There was no increase in apoptosis with any drug in the absence of HRP/H2O2. These results indicate that this assay is unable to reliably predict the ability of different types of drugs to cause agranulocytosis. This is not a surprising result given that different drugs may induce agranulocytosis by different mechanisms.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:575087 CAPLUS
DN 137:140432
TI Preparation of pyridoindoles as human serotonin receptor 5-HT2C agonists and 5-HT2A antagonists
IN Robichaud, Albert J.; Fevig, John M.; Mitchell, Ian S.; Lee, Taekyu; Chen, Wenting; Cacciola, Joseph
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 409 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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PI WO 2002059129	A2	20020801	WO 2001-US49371	20011219
WO 2002059129	A3	20030130		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM